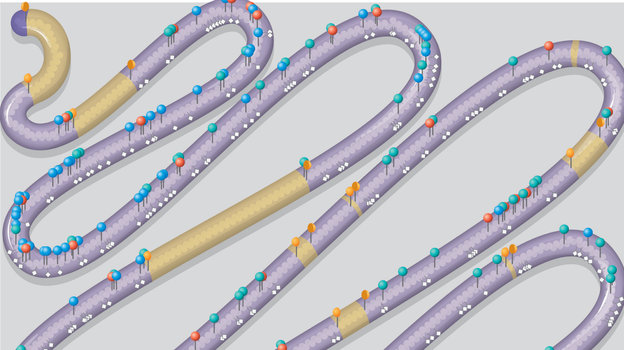
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Custom Chromo: First Yeast Chromosome Built From Scratch

The research team used yeast chromosome No. 3 as the model for their biochemical stitchery. Pins and white diamonds in the illustration represent "designer changes" not found in the usual No. 3; yellow stretches represent deletions.



*Lucy Reading-Ikkanda*

Using the labor of dozens of undergraduate students, scientists have built a customized yeast chromosome from scratch.

It's a milestone in the rapidly growing field of synthetic biology, where organisms can be tailored for industrial use. In this case, the near-term goal is to understand the genetics of yeast, and eventually the genetics of us. This was quite an undertaking. Yeast have about 6,000 genes packed in 16 tidy bundles called chromosomes. Each chromosome is an enormous molecule of DNA packed in proteins.

[](http://www.npr.org/templates/story/story.php?storyId=127010591)

[**Scientists Reach Milestone On Way To Artificial Life**](http://www.npr.org/templates/story/story.php?storyId=127010591)

The story started about 15 years ago, when [Ronald Davis](https://med.stanford.edu/profiles/ronald-davis), a prominent Stanford University geneticist, stood up at a science meeting and declared that someday someone would build a yeast chromosome from scratch.

[Research News](http://www.npr.org/sections/research-news/)

[**Genetic First: Bacterium's Code Built from Scratch**](http://www.npr.org/templates/story/story.php?storyId=18393850)

"I remember saying to myself, 'Why on Earth world anyone do that?' " says geneticist [Jef Boeke](http://www.mbg.jhmi.edu/Pages/people/profile.aspx?PID=2), who was then working at Johns Hopkins University.

[](http://www.npr.org/templates/story/story.php?storyId=18393850)

About 10 years later, Boeke bumped into a Hopkins colleague, [Srinivasan Chandrasegaran](http://www.jhsph.edu/faculty/directory/profile/1328/Chandrasegaran/Srinivasan), at a coffee shop and they started talking about huge molecules they could synthesize. Boeke suggested they could build a yeast chromosome from scratch, "and he looks at me incredulous and said, ' Really? We've got to do it! We've got to do it,' " Boeke recalls. Chandrasegaran "was practically jumping up and down with excitement," Boeke says.

[Science](http://www.npr.org/sections/science/)

At first, Boeke tried to buy some of the DNA strands they wanted to use from a commercial outfit. But the first small batch took nearly a year to arrive.

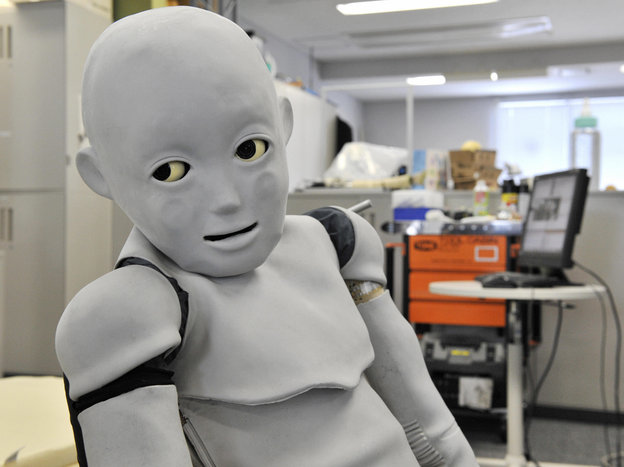
**T**he students are learning techniques that are transferable to many other organisms and, because you have this fantastic power to modify DNA, it comes with responsibilities.

*- Debra Mathews*

"I realized I would be dead long before the project could ever be completed," he says. "So it suddenly hit me that there were all these students on the undergraduate campus who would be dying for a great research opportunity."

Boeke and his colleagues put together a class, called Build-A-Genome, and got undergraduates at Hopkins to do the painstaking labor of constructing long strings of DNA. These would eventually become segments of their yeast chromosome.

They [published](http://www.sciencemag.org/content/early/2014/03/26/science.1249252.abstract) evidence of their success Thursday in *Science*. The team built yeast chromosome No. 3 from scratch. (More precisely, they assembled the DNA strand that's the core of the chromosome, and put it in a yeast cell, which then proceeded to package it up in proteins and coil it into the compact structure of a chromosome.)



To make the chromosome useful for research, they've deleted some parts of the DNA that they believe are not essential, "and then we add a number of bells and whistles to the chromosome, that we think will make for a more interesting version that we can play evolutionary games with in the laboratory," Boeke says.

They're interested in going after big questions, such as what is it in the DNA that keeps one species separate from the next.

Of course, this deep manipulation of DNA also raises ethical questions — about everything from patenting life-forms, to the potential misuse of biotechnology for weapons or other nefarious purposes. So part of the class involved an ethics discussion, led by Debra Mathews, a bioethicist at Johns Hopkins.

"It's not just this particular project," Mathews says, noting that yeast aren't likely to be the starting point for anything that might harm humans. But, she adds, "the students are learning techniques that are transferable to many other organisms and, because you have this fantastic power to modify DNA, it comes with responsibilities."

If scientists can build all 16 yeast chromosomes from scratch, they'd have an entire set of yeast genes to tinker with. That could be a big advance for understanding how genes work, in yeast — and by extension in humans. We have similar chromosomes.

"You can look at a car and you think you understand a car," Davis says. "But if you really understand a car you should be able to build one."

Jef Boeke is now working to build other yeast chromosomes. He recently became director of the Institute for Systems Genetics at New York University's Langone Medical Center, and he's become part of an [international consortium](http://syntheticyeast.org/) that aims to build the remaining 15 yeast chromosomes from scratch. So far, people were working on all but one of them.